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Expression of human alpha 2-macroglobulin cDNA in baby hamster kidney fibroblasts: secretion of high levels of active alpha 2-macroglobulin.

Boel E, Kristensen T, Petersen CM, Mortensen SB, Gliemann J, Sottrup-Jensen L.

Bioscience, Novo Nordisk A/S, Bagsvaerd, Denmark.

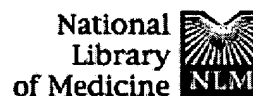
Human alpha 2-macroglobulin (alpha 2M) is a unique 720-kDa proteinase inhibitor with a broad specificity. Unlike most other proteinase inhibitors, it does not inhibit proteolytic activity by blocking the active site of the proteinase. During complex formation with a proteinase, alpha 2M entraps the proteinase molecule in a reaction that involves large conformational changes in alpha 2M. We describe the molecular cloning of alpha 2M cDNA from the human hepatoblastoma cell line HepG2. The cDNA was subcloned under control of the adenovirus major late promoter in a mammalian expression vector and introduced into the baby hamster kidney (BHK) cell line. Transformed clones were isolated and tested for production of human alpha 2M with a specific enzyme-linked immunosorbent assay. Human recombinant alpha 2M (r alpha 2M), secreted and purified from isolated transfected BHK cell lines, was structurally and functionally compared to alpha 2M purified from human serum. The results show that r alpha 2M was secreted from the BHK cells as an active proteinase-binding tetramer with functional thiol esters. Cleavage reactions of r alpha 2M with methylamine and trypsin showed that the recombinant product, which was correctly processed at the N-terminus, exhibited molecular characteristics similar to those of the human serum derived reference. Moreover, r alpha 2M-trypsin complex bound to purified human placental alpha 2M receptor with an affinity indistinguishable from that of a complex formed from serum-derived alpha 2M and trypsin.

PMID: 1694456 [PubMed - indexed for MEDLINE]

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Prostate specific antigen-alpha 2-macroglobulin complexes in prostate cancer patient sera.

Heeb MJ, Espana F, Gittes RF, Griffin JH.

Scripps Research Institu

Quantitative immunoblotting of prostate specific antigen was in patient sera with little of it being free. Inhibitors in patient sera complexes. Each complexed with alpha 2-macroglobulin. With alpha 2-macroglobulin, approximately 40% free antigen, approximately 20% complexed. Prostate specific antigen reacts with alpha 2-macroglobulin in plasma and cancer patients.

PMID: 8624498 [PubMed]

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Prostate cancer patient sera revealed that most prostate specific antigen was complexed with alpha 2-macroglobulin. Prostate specific antigen with these protease inhibitors was complexed with the respective purified alpha 2-macroglobulin from patient sera by absorption with alpha 2-macroglobulin. As added to normal plasma, complexes formed. After 1 hr, the distribution was approximately 40% free antigen, approximately 20% complexed with alpha 2-macroglobulin, and approximately 40% complexed with alpha 2-macroglobulin. These data show that prostate specific antigen reacts with alpha 2-macroglobulin in plasma and cancer patients.

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